REMARKS

This amendment is in response to the non-final Office Action mailed September 22, 2004. Previously, Claims 1-20 were pending. In the instant amendment, Claim 20 has been cancelled without prejudice. Claims 11-14, 17 and 19 have been amended. After entry of the instant amendment, Claims 1-19 will be pending and under consideration.

I. THE AMENDMENTS TO THE SPECIFICATION

The specification has been amended at page 4 to recite, in relevant part, "G190S" instead of "G109S." Support for this amendment, which corrects an inadvertent typographical error, can be found, for example, in the specification, at page 4, lines 1-3, 12 and 24, at page 5, lines 1-5, at page 14, lines 4-9, and Figure 2 and Figure 7. This amendment does not introduce any new matter. Entry of the amendments to the specification is respectfully requested.

II. THE AMENDMENTS TO THE CLAIMS

Claim 20 has been cancelled without prejudice to Applicants' right to pursue the subject matter of the cancelled claim in one or more related continuation, divisional or continuation-in-part application(s).

Claim 11 has been amended to be an independent claim, and Claims 12-14 have been amended to depend from Claim 11. Claims 17 and 19 have been amended. Support for the amendments to Claims 11-14, 17 and 19 can be found, for example, in Claims 11-14, 17 and 19 as originally filed, and in the specification at page 4, lines 25-32, at page 5, lines 1-5, at page 14, lines 4-9, at page 30, lines 18-22, and Figure 2 and 7.

The amendments do not introduce any new matter and they are fully supported by the instant specification and the claims as originally filed. Entry and consideration of the amendments is respectfully requested. No amendment fee is believed to be due.

III. THE REJECTION OF CLAIMS 12, 14, 17 AND 19 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 12, 14, 17 and 19 stand rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. Specifically, the Patent Office contends that recitation of detecting the presence of absence of P236L is contradictory to the language of Claim 1, from which Claims 12, 14, 17 and 19 ultimately depend. Without acquiescing to the propriety of this

rejection, Applicants have amended Claims 11, 12, 14, 17 and 19 in a manner that has rendered moot the rejection of these claims. Accordingly, Applicants respectfully request withdrawal of the rejection of Claims 12, 14, 17 and 19 as indefinite under 35 U.S.C. § 112, second paragraph.

IV. THE REJECTION OF CLAIMS 1-19 UNDER 35 U.S.C. § 102(b)

Claims 1-19 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Whitcomb, WO 99/61658 ("Whitcomb"). Claims 1-13 and 15-18 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Richman *et al.*, J. Virology, March 1984, 68(3):1660-1666 ("Richman *et al.*"). Applicants respectfully transverse.

A. The Legal Standard

The standard governing anticipation under 35 U.S.C. § 102 requires strict identity. *See* M.P.E.P. § 2131. Thus, "for a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." *See In re Bond*, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990). Anticipation is not shown even when the differences between the claims and the cited reference are allegedly "insubstantial" and any missing elements could be supplied by the knowledge of one skilled in the art. *See Structural Rubber Prod. Co. v. Park Rubber Co.*, 223 U.S.P.Q. 1264 (Fed. Cir. 1984). Furthermore, in *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 U.S.P.Q. 253 (Fed. Cir. 1985), the Federal Circuit explained that even if the prior art teaches "substantially the same thing" as the claimed invention, the reference still cannot anticipate the invention. Thus, a cited reference must describe each and every claim limitation in order to anticipate the invention as claimed.

B. Richman *et al.* Does Not Teach Each and Every Element of Claims 1-13 and 15-18

Applicants submit that Richman *et al.* does not teach each and every element of Claims 1-13 and 15-18. Richman *et al.* purports to teach that HIV-1's resistance to nevirapine, one of non-nucleoside reverse transcriptase inhibitors ("NNRTI"), is associated with certain mutations in HIV-1 reverse transcriptase. Particularly, Richman *et al.* teaches that mutations at amino acid position 103, 106 or 181 of HIV-1 reverse transcriptase result in resistance to certain NNRTIs. However, Richman *et al.* teaches only the effects of the mutations on drug resistance. Richman *et al.* in no way discusses the effects of the mutations on the replication capacity of an HIV-1 virus, and certainly fails to teach that any mutation in

HIV-1 reverse transcriptase is associated with impaired viral replication capacity. Moreover, none of the experiments described in Richman *et al.* measures the replication capacity of an HIV-1 virus having mutations in its reverse transcriptase. As such, Richman *et al.* does not and cannot teach either a method for determining whether an HIV-1 has an increased likelihood of having impaired replication capacity, or a method for determining whether a subject has an HIV-1 with an increased likelihood of having an impaired replication capacity, by determining the presence or absence of a mutation associated with impaired replication capacity of HIV-1 reverse transcriptase. Applicants, therefore, submit that Richman *et al.* does not anticipate Claims 1-13 and 15-18, and respectfully request that the rejection of these claims under 35 U.S.C. § 102(b) be withdrawn.

C. Whitcomb Does Not Teach Each and Every Element of Claims 1-19

Applicants submit that essentially for the same reasons as discussed above, Whitcomb does not teach each and every element of Claims 1-19. For example, Whitcomb does not teach that the presence of the mutations of HIV-1 reverse transcriptase cited in Claims 1-19 is associated with impaired replication capacity of the virus. Instead, Whitcomb teaches that mutations at amino acid position 101, 103, 106, 109, 181, 189, 227 and 236 correlate with resistance to antiviral therapy. Therefore, Whitcomb does not teach each and every element of Claims 1-19 and cannot anticipate Claims 1-19.

In view of the foregoing, Applicants respectfully submit that the rejection of Claims 1-19 under 35 U.S.C. § 102(b) be withdrawn.

V. THE REJECTION OF CLAIMS 1-19 UNDER 35 U.S.C. § 103

Claims 14 and 19 stand rejected under 35 U.S.C. § 103 as allegedly being obvious over Richman *et al.*, J. Virology, March 1984, 68(3):1660-1666 ("Richman *et al.*"), in view of Whitcomb *et al.*, WO 99/61658 ("Whitcomb *et al.*"). Applicants respectfully traverse the rejection on the ground the Patent Office has not presented a *prima facie* case for obviousness in that the combined references do not teach or suggest each and every element of the invention as presently claimed.

A. The Legal Standard

To reject a claim under 35 U.S.C. § 103(a), the PTO bears the initial burden of showing an invention to be prima facie obvious over the prior art. *See In re Bell*, 26U.S.P.Q.2d 1529 (Fed. Cir. 1992). If the PTO cannot establish a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent. *See In re*

Oetiker, 24 U.S.P.Q.2d 1443 (Fed. Cir. 1992). The PTO must meet a three-part test to render a claimed invention *prima facie* obvious.

To begin with, the prior art references cited by the PTO must provide "motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant." *See In re Kotzab*, 55 U.S.P.Q.2d 1316 (Fed. Cir. 2000). Where one reference is relied upon by the PTO, there must be a suggestion or motivation to modify the teachings of that reference. *See id.* Where an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *See WMS Gaming Inc. v. International Game Technology*, 51U.S.P.Q.2d 1386 (Fed. Cir. 1999). The suggestion may be found in implicit or explicit teachings within the references themselves, from the ordinary knowledge of one skilled in the art, or from the nature of the problem to be solved. *See id.*

Second, the prior art references cited by the PTO must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. *See In re Dow Chemical*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). The expectation of success, like the motivation to combine two prior art references, must come from the prior art, not the applicant's disclosure. *See id.*

Finally, the PTO must show that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. *See In re Gartside*, 53 U.S.P.Q.2d 1769 (Fed. Cir. 2000). If any one of these three factors is not met, the PTO has failed to establish a *prima facie* case of obviousness and the applicant is entitled to grant of a patent without making any affirmative showing of non-obviousness.

B. The Cited References Fail to Establish a *Prima Facie* Case of Obviousness against Amended Claims 14 and 19

In support of its rejection of Claims 14 and 19 under 35 U.S.C. § 103, the Patent Office alleges that since Richman *et al.* discloses nevirapine resistance mutations of HIV-1 reverse transcriptase-K103N, G190A and Y181C, and Whitcomb discloses drug resistance mutation of HIV-1 reverse transcriptase P225H, it would have been obvious to use the mutations disclosed by Whitcomb in the method of Richman *et al.* Therefore, the Patent Office contends that Claims 14 and 19 are *prima facie* obvious over Richman *et al.* in view of Whitcomb.

Applicants respectfully submit that the Patent Office has failed to establish a *prima facia* case of obviousness against Claims 14 and 19. Neither Richman *et al.* nor Whitcomb

teaches or suggests that such mutations might correlate with impaired viral replication capacity of an HIV-1 virus having these mutations in its reverse transcriptase. As such, the combined disclosure of Richman *et al.* and Whitcomb fails to teach or suggest either a method for determining whether an HIV-1 has an increased likelihood of having impaired replication capacity or a method for determining whether a subject has an HIV-1 with an increased likelihood of having an impaired replication capacity, comprising determining the presence or absence of a mutation associated with impaired replication capacity of HIV-1 reverse transcriptase. Accordingly, Richman *et al.* and Whitcomb, either alone or in combination, fail to teach or suggest each and every element of Claims 14 and 19. Thus, Claims 14 and 19 are not obvious over Richman *et al.* in view of Whitcomb.

Therefore, Applicants respectfully request that the rejection of Claims 14 and 19 under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants respectfully request that the Examiner reconsider this application with a view towards allowance. Applicants submit that Claims 1-19 satisfy all of the criteria for patentability and are in condition for allowance. The Examiner is invited to call the undersigned attorney at 650-739-3939 if a telephone call could help resolve any remaining items.

No fees, other than that for the Petition for Extension of Time, are believed due in connection with this response. However, pursuant to 37 C.F.R. §1.136 (a)(3), the Commissioner is authorized to charge all required fees, fees under 37 C.F.R. §1.17 and all required extension of time fees, or credit any overpayment, to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

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